The Psychobiology of Posttraumatic Stress Disorder

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This review summarizes the current state of our knowledge of the psychobiology of posttraumatic stress disorder (PTSD). People with PTSD develop an enduring vigilance for and sensitivity to environmental threat. They have difficulty in properly evaluating sensory stimuli and responding with appropriate levels of physiologic and neurohormonal arousal. The inappropriate mobilization of biological emergency responses to innocuous stimuli is mirrored psychologically in an inability to properly integrate memories of the trauma and in a fixation on the past. The biological dysregulation of PTSD can be measured on physiologic, neurohormonal, immunologic, and functional neuroanatomical levels. The developmental level at which the trauma occurs affects the nature and extent of psychobiological disruptions. The availability of neuroimaging for documenting structural and functional abnormalities in PTSD has opened up new ways for understanding the neuronal filters concerned with the interpretation of sensory information in PTSD. These studies have produced a number of unexpected findings, which may alter how we conceptualize PTSD and which may force us to reevaluate appropriate therapeutic interventions. *(J Clin Psychiatry 1997;58[suppl 9]:16–24)*

The brain serves as an analyzing and amplifying device for maintaining us in our internal and external environment.[1] Different systems in the brain are involved in different functions, ranging from the regulation of oxygen intake to the categorization of incoming information necessary for making complex, long-term decisions. A large number of complex brain structures, the brain stem, the thalamus, the basal ganglia, the limbic system, the cerebellum, and the neocortex, constitute a great collection of systems that filter and process information.

These systems need to function in harmony to allow the individual to decide what sensory stimuli are relevant and which ones are not, to weigh a range of options for action, to anticipate the outcome of one's actions, to concentrate on a particular task until it has been accomplished, and then to let go and attend to other stimuli. People with posttraumatic stress disorder (PTSD) have a host of problems in carrying out precisely these functions.[2]

The brain stem, hypothalamus, and pituitary gland control basic biological functions such as temperature regulation, oxygen intake, blood glucose levels, and production of hormones in the thyroid and adrenal glands. Their regulatory functions are affected by input from the limbic system and the neocortex. The limbic system has functions related to self-preservation and procreation, parental care, and play.[1] The neocortex is primarily oriented toward the external world, and is involved in problem solving, learning, and complex stimulus discriminations. In addition, it plays a critical role by mediating the transcription of subjective states into communicable language to self and others.

THE SYMPTOMATOLOGY OF PTSD

When Abram Kardiner (1941) first gave detailed descriptions of the effect of war trauma, he noted that sufferers from "traumatic neuroses" develop an enduring vigilance for and sensitivity to environmental threat: they developed a chronic psychobiological dysregulation.[3] Kardiner stated that the physiologic hyperarousal characteristic of PTSD occurs not only in response to combat sounds: many of his patients also suffered from sensitivity to temperature, pain, and sudden tactile stimuli, as well. "These patients cannot stand being slapped on the back abruptly; they cannot tolerate a misstep or a stumble. From a physiologic point of view, there exists a lowering of the threshold of stimulation, and from a psychological point of view, a state of readiness for fright reactions."[3] Contemporary research on the biology of PTSD has confirmed that there are profound and persistent alterations in physiologic reactivity and stress hormone secretion in people with PTSD. These findings have profound implications for understanding the nature of the disorder and for designing appropriate treatment.

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Physiologic Arousal

PTSD is not an issue of simple conditioning. Most people who have been exposed to a tragedy become distressed when they are reminded of it, whether they develop PTSD or not. Pitman et al. have pointed out that the critical issue in PTSD is that the stimuli that cause people to overreact may not be conditional enough: a variety of triggers not directly related to the traumatic experience may come to precipitate extreme reactions.[4] The persistence of intrusive thoughts and images, by means of the process of kindling, sets up a chronically disordered pattern of arousal, in which the patient reacts to a host of reminders with a physiologic intensity appropriate to the original trauma.

In an apparent attempt to compensate for their chronic hyperarousal, traumatized people seem to shut down—on a behavioral level, by avoiding stimuli that remind them of the trauma, on a psychobiological level, by emotional numbing, which may extend to both trauma-related and everyday experience.[5] Over time, people with chronic PTSD come to suffer from numbing of responsiveness to the environment, intermittent hyperarousal in response to emotionally arousing stimuli, and nonspecific hyperarousal to intense but neutral stimuli. Hence, abnormal psychophysiologic reactions in PTSD occur on two different levels: (1) in response to specific reminders of the trauma and (2) in response to intense, but neutral stimuli, such as loud noises. This indicates that people with PTSD suffer from a loss of stimulus discrimination.

Conditional Responses to Specific Stimuli

People with PTSD suffer from heightened physiologic arousal in response to sounds, images, and thoughts related to specific traumatic incidents. They respond to such reminders with significant increases in heart rate, skin conductance, and blood pressure.[6–8] The highly elevated autonomic responses to reminders of traumatic experiences that happened years, and sometimes decades, ago illustrate the intensity and timelessness with which these memories continue to affect current experience.[4]

Situations or medications that stimulate heightened autonomic arousal may precipitate visual images and affect states associated with prior traumatic experiences. The administration of drugs such as lactate[9] or yohimbine[10] to patients with PTSD (but not controls) tends to precipitate panic attacks, flashbacks of earlier trauma, or both. In our laboratory, approximately 20% of PTSD subjects responded to acoustic startle stimuli with flashbacks.[11]

Hyperarousal to Intense but Neutral Stimuli/ Loss of Stimulus Discrimination

Excessive stimulation of the CNS at the time of the trauma may result in permanent neuronal changes that have a negative effect on learning, habituation, and stimulus discrimination.[12] These neuronal changes do not depend on actual exposure to reminders of the trauma for expression. The abnormal startle response characteristic of PTSD is one example of this phenomenon. Several studies have demonstrated abnormalities in habituation to the acoustic startle response (ASR) in PTSD.[13,14] Shalev et al.[13] found a failure to habituate both to CNS and autonomic nervous system–mediated responses to ASR in 93% of the PTSD group, compared with 22% of the control subjects. Interestingly, people who previously met criteria for PTSD, but no longer do so now, continue to show failure of habituation of the ASR (van der Kolk BA. 1994. Unpublished data), which raises the question of whether abnormal habituation to acoustic startle is a marker of, or a vulnerability factor for, developing PTSD. Thus, the inability of people with PTSD to properly integrate memories of the trauma and, instead, their being mired in a continuous reliving of the past, is mirrored physiologically in the misinterpretation of innocuous stimuli, such as acoustic startle, as potential threats.

The failure to habituate to acoustic startle suggests that traumatized people have difficulty evaluating sensory stimuli and mobilizing appropriate levels of physiologic arousal.[13] This is further illustrated by a study of McFarlane and colleagues.[15] Using event-related potentials (ERPs), they found that people with PTSD (1) were unable to differentiate relevant from irrelevant stimuli, (2) attended less to affectively neutral, but existentially relevant events, and (3) as a consequence of this relative lack of responsiveness, needed to apply more effort than nontraumatized people to respond to current experience (as reflected in a delayed reaction time). These studies suggest that people with PTSD have difficulty neutralizing stimuli in their environment in order to attend to relevant tasks. To compensate, they tend to shut down, and fail to attend to ordinary, nontraumatic stimuli. The price for shutting down is decreased involvement in ordinary, everyday life.

Chronic physiologic arousal, and the resulting failure to regulate autonomic reactions to internal or external stimuli, affects people's capacity to utilize emotions as signals. Krystal[16] first noted that the emotions of people with PTSD do not seem to serve their usual alerting function, namely, as warning signals to take adaptive action. In patients with PTSD, emotional arousal and goal-directed action often are dissociated from each other. They no longer use arousal as a cue to pay attention to incoming information. Instead, they tend to go immediately from stimulus to response without first being able to figure out the meaning of what is going on and respond with flight or fight reactions.

NEUROHORMONAL RESPONSES IN PTSD

Background

PTSD develops following exposure to events that are intensely distressing. Intense stress is accompanied by

the release of endogenous, stress-responsive neurohormones, such as cortisol, epinephrine and norepinephrine (NE), vasopressin, oxytocin, and endogenous opioids. These stress hormones help the organism mobilize the required energy to deal with the stress, ranging from increased glucose release to enhanced immune function. In a well-functioning organism, stress produces rapid and pronounced responses in hormonal levels, which rapidly return to baseline after the threat has passed. Chronic and catastrophic stress has been shown to inhibit the effectiveness of the stress response and induces desensitization.[17] Most studies of neurohormone function in PTSD show responses that are in the opposite direction from those of the ordinary stress response.

Catecholamines

The neurohormone NE is critical for alerting the organism to deal with threat and for initiating fight/flight behaviors. In addition, it plays a significant role in memory consolidation. Neuroendocrine studies of Vietnam veterans with PTSD have found good evidence for chronically increased sympathetic nervous system activity in PTSD. One study[18] found elevated 24-hour excretions of urinary NE and epinephrine in PTSD combat veterans compared with patients with other psychiatric diagnoses. Studies have demonstrated an apparently compensatory down-regulation of adrenergic receptors in response to increased NE levels: one found decreased platelet α_2-adrenergic receptors in combat veterans with PTSD,[19] while another found an abnormally low α_2-adrenergic receptor–mediated adenylate cyclase signal transduction.[20] In a recent study, Southwick et al.[10] used yohimbine injections (0.4 mg/kg), which activate noradrenergic neurons by blocking the α_2-autoreceptor, to study noradrenergic neuronal dysregulation in Vietnam veterans with PTSD. Yohimbine precipitated panic attacks in 70% of subjects and flashbacks in 40% (for a more extensive discussion of catecholamines in PTSD, see Murburg[21]).

The Hypothalamic-Pituitary-Adrenal (HPA) Axis

The HPA axis system plays a different role in the stress response. The cortisol release from the adrenal, which is the standard response to exposure to stress, is regulated by adrenocorticotropin-releasing hormone (ACTH) release from the pituitary, which in turn is primarily regulated by corticotropin-releasing factor release from the hypothalamus. Glucocorticoids and catecholamines seem to modulate each other's effects: in acute stress, cortisol helps regulate stress hormone release via a negative feedback loop to the hippocampus, hypothalamus, and pituitary.[22] Yehuda has proposed that the function of the glucocorticoid system is to shut off the other biological reactions that are initiated after immediate exposure to acute stress.[23] This would imply that cortisol is basically an "antistress" hormone. Thus, she proposes that simultaneous activation of catecholamines and glucocorticoids stimulates active coping behaviors, while increased arousal in the presence of low glucocorticoid levels would provoke undifferentiated fight or flight reactions."[3]

Chronic exposure to stress permanently alters how an organism deals with its environment on a day-to-day basis. While acute stress activates the HPA axis and increases glucocorticoid levels, organisms adapt to chronic stress by activating a negative feedback loop that results in (1) decreased resting glucocorticoid levels in chronically stressed organisms, (2) decreased glucocorticoid secretion in response to subsequent stress, and (3) increased concentration of glucocorticoid receptors in the hippocampus.[24-26]

In a series of studies, Rachel Yehuda and colleagues have found (1) low urinary cortisol, (2) hypersuppression of cortisol release in response to the dexamethasone suppression test in patients with PTSD, and (3) increased numbers of lymphocyte glucocorticoid receptors in Vietnam veterans with PTSD. Interestingly, the number of glucocorticoid receptors was proportional to the severity of PTSD symptoms.[23,24,27]

Two different studies support the notion that a *low* cortisol response to stress makes people vulnerable to developing PTSD. Heidi Resnick and her colleagues[28] studied acute cortisol response to trauma by measuring cortisol in the blood samples of 20 acute rape victims. Three months later, a prior trauma history was taken, and the subjects were evaluated for the presence of PTSD. Victims with a prior history of sexual abuse were significantly more likely to have developed PTSD 3 months following the rape than rape victims who did not have a history of sexual abuse. Cortisol levels shortly after the rape were correlated with histories of prior assaults: the mean initial cortisol level of individuals with a prior assault history was 15 µg/dL compared with 30 µg/dL in individuals without it. In a second study, McFarlane,[29] studying predictors of the development of PTSD in car accident victims, found that low cortisol levels in the emergency room, right after the accident, predicted the development of PTSD 3 months later.

These studies suggest that failure to mount an adequate cortisol response to acute stress may interfere with the organism's capacity to integrate the experience, setting the stage for continued preoccupation with traumatic memories and the ultimate development of PTSD.

Altered Immune Function

Animal and human research indicates that low concentrations of cortisol are associated with enhanced immune function. Many chronic PTSD patients have multiple physical problems and a high degree of use of medical services.[30] In my own clinical practice, I seem to see a disproportionately high prevalence of autoimmune diseases in women with histories of sexual abuse.

Table 1. Biological Abnormalities in PTSD

Psychophysiologic
Extreme autonomic responses to stimuli reminiscent of the trauma
Nonhabituation to startle stimuli
Reduced response to event-related potentials
Response to sound intensifies below threshold
Decreased EEG cortico-corticol synchronization in children
Neurotransmitter
Noradrenergic
Elevated urinary catecholamines
Increased MHPG to yohimbine challenge
Reduced platelet MAO activity
Down-regulation of adrenergic receptors
Serotonergic
Decreased serotonin activity in traumatized animals
Best pharmacologic responses to serotonin selective uptake inhibitors
Endogenous opioids—increased opioid response to stimuli reminiscent of trauma
HPA axis
Decreased resting glucocorticoid levels
Decreased glucocorticoid response to stress
Down-regulation of glucocorticoid receptors
Hyperresponsiveness to low-dose dexamethasone
Memory
Amnesias and hyperamnesias
Traumatic memories precipitated by noradrenergic stimulation, physiologic arousal, reminders
Memories generally sensorimotor rather than semantic
Neuroanatomical
Decreased hippocampal volume
Activation right amygdala and parahippocampal structures during flashbacks
Activation right sensory areas during flashbacks
Decreased activation of Broca's area during traumatic exposure
Marked hemisphere lateralization
Decreased left hemisphere cortical synchronization in abused children
Miscellaneous
Traumatic nightmares often not oneiric but extract replicas of visual elements of trauma; may occur in stage II or III sleep
Impaired psychoimmunologic function

This impression led us to conduct immunologic research on 12 women with documented histories of childhood sexual abuse and 12 control subjects.[31] Results demonstrated that immune function was almost the same in both groups—except for CD45 lymphocytes, known as the "memory cells" of the immune system. The abnormality involved the RO:RA ratio—the ratio of T-cells that remember the previous challenges versus the number of naive T-cells ready to respond to new threats. In other words, these sexually abused women have been exposed to a greater number of immunologic challenges and thus have an increased propensity to remember and respond to immunologic challenges in the direction of trauma. These patients with PTSD immunologically resembled patients with illnesses characterized by a lower RO:RA ratio, such as rheumatoid arthritis, systemic lupus erythematosus, and sarcoid.

Serotonin

The serotonin system also plays a role in modulating noradrenergic responsiveness and arousal. Low serotonin in animals is related to an inability to modulate arousal, as exemplified by an exaggerated startle, and increased arousal in response to novel stimuli, handling, or pain.[32] Depue and Spoont[33] characterize the phenomena produced in animals by serotonin depletion as hyperirritability, hyperexcitability, and hypersensitivity, and an "exaggerated emotional arousal and/or aggressive display (though not necessarily attack) to relatively mild stimuli. . . ." These behaviors bear a striking resemblance to what is observed in people with PTSD. Decreased serotonin function has also been correlated with hostility, impulsivity, and self-directed aggression in patients with depression and with borderline personality disorder,[34,35] a diagnostic group with frequent histories of severe childhood trauma.[36]

Serotonin mediates a behavioral inhibition system in the brain that helps suppress behaviors that are motivated by emergencies or by previous reward.[33,37,38] Serotonin reuptake inhibitors have been found to be effective psychopharmacologic intervention for the involuntary preoccupation with traumatic memories.[39] It is likely that serotonin plays a role in the capacity to monitor the environment flexibly and to respond with behaviors that are situation appropriate, instead of reacting to internal stimuli that are irrelevant to current demands. Stress-induced serotonin dysfunction may lead to impaired function of the behavioral inhibition system, which may be related to various behavioral problems seen in PTSD, including impulsivity, aggressive outbursts, compulsive re-enactment of trauma-related behavior patterns, and a seeming inability to learn from past mistakes.

Decreased serotonin in humans has repeatedly been correlated with impulsivity and aggression.[35,40] The literature tends to readily assume that these relationships are based on genetic traits. However, studies of impulsive, aggressive, and suicidal patients seem to find at least as robust an association between those behaviors and histories of childhood trauma.[41–43] It is likely that both temperament and experience affect relative CNS serotonin levels.

In order to test serotonergic contributions to trauma-related symptomatology, Southwick et al.[44] administered 1 mg/kg of *m*-CPP, a 5-HT agonist, to 26 Vietnam veterans with PTSD. Thirty-one percent of the subjects experienced a panic attack, and 27% had a flashback. These figures were comparable to those following the administration of yohimbine, which acts solely on the noradrenergic system. There was almost no overlap between the subjects who had these reactions to *m*-CPP and those who did to yohimbine.[44] This suggests that multiple neurotransmitters are involved in these complex PTSD symptoms (Table 1).

Developmental Level and the Psychobiological Effects of Trauma

In recent years a small prospective literature has emerged that documents the differential effects of trauma at various age levels. Childhood abuse manifests itself

through an array of psychiatric problems, such as depression, anxiety, suicidal ideation, aggressive-impulsivity, delinquency, and substance abuse.[45,46] It is increasingly recognized that chronic intrafamilial abuse tends to produce complex posttraumatic syndromes, which involve chronic affect dysregulation, destructive behavior against self and others, learning disabilities, dissociative problems, somatization, and distortions in concepts about self and others.[45,47]

Neuroendocrine abnormalities and cerebral lateralization. Frank Putnam and his group's prospective studies are showing major neuroendocrine disturbances in sexually abused girls compared with normals, particularly in the areas of immune, corticosteroid, and thyroid functions.[48-50] Martin Teicher and his colleagues[51-56] have produced substantial evidence that early traumatic experience affects the development of the cerebral cortex and limbic system. In a study of limbic system abnormalities, they found that childhood physical abuse was associated with a 38% increase in limbic system abnormalities, sexual abuse with a 49% increase, and combined abuse with a 113% increase. These scores were elevated only if the trauma occurred before age 18.

In a study of EEG abnormalities, Ito and colleagues[56] found an association between abuse history and neurologic abnormalities. Abused children had a greater incidence of electrophysiologic abnormalities than nonabused children. Abused and nonabused patients differed only in the prevalence of left hemisphere abnormalities. Left hemisphere deficits were seven times more common than right hemisphere deficits. Their findings suggest that the two hemispheres may function more autonomously in patients with childhood abuse. These findings are consistent with research showing that abused children have significant problems in the dominant hemisphere function of language development.[57]

Neuroimaging Studies in PTSD

During the past few years, the availability of neuroimaging for documenting structural and functional abnormalities in PTSD has opened up new ways of understanding the neurobiological processes involved in PTSD. The emerging body of knowledge from these studies is stimulating an interest that is complementing the study of the neurochemicals involved in the organism's response to overwhelming threat. Neuroimaging has promoted a new focus on the neuronal *filters* concerned in the *interpretation* of sensory information: the interactions between the various parts of the CNS that process and interpret the meaning of incoming information, such as the amygdala, hippocampus, corpus callosum, anterior cingulate, and prefrontal cortex. As of late 1996, there have been four published studies utilizing neuroimaging of patients with PTSD.[58-61] Two more studies have been completed and are in press, while several other studies are currently under way (Liberzon I. 1996. Unpublished data).

Hippocampal volume. Three studies, done in different laboratories, have shown that people with PTSD have decreased hippocampal volumes compared with matched controls: Bremner and his colleagues[60] found that Vietnam combat veterans with PTSD had an 8% reduction in the volume of their right hippocampus compared with veterans without such symptoms. Stein et al.[61] found a 7% reduction in hippocampal volume in women with PTSD who had suffered repeated childhood sexual abuse. Gurvitz et al.[59] found that Vietnam veterans with the most intense combat exposure and with the most severe PTSD had an average shrinkage of 26% in the left hippocampus and 22% in the right hippocampus, compared with veterans who saw combat but had no symptoms. The severity of their PTSD was directly proportional to the degree of hippocampal shrinkage.

Symptom provocation studies. Rauch and colleagues conducted a positron emission tomography study of patients with PTSD in which they were exposed to vivid, detailed narratives of their own traumatic experiences.[58] During exposure to the script of their traumatic experiences, these subjects demonstrated heightened activity only in the right hemisphere, specifically, in the areas that are most involved in emotional arousal: the amygdala, insula, and medial temporal lobe. Activation of these structures was accompanied by heightened activity in the right visual cortex. While people were exposed to their traumatic scripts, there was a significant decrease in activation of the left inferior frontal area, Broca's area, which is thought to be responsible for translating personal experiences into communicable language (Figure 1). The study by Shin et al.,[62] utilizing a slightly different paradigm, essentially confirmed these findings in a different trauma population.

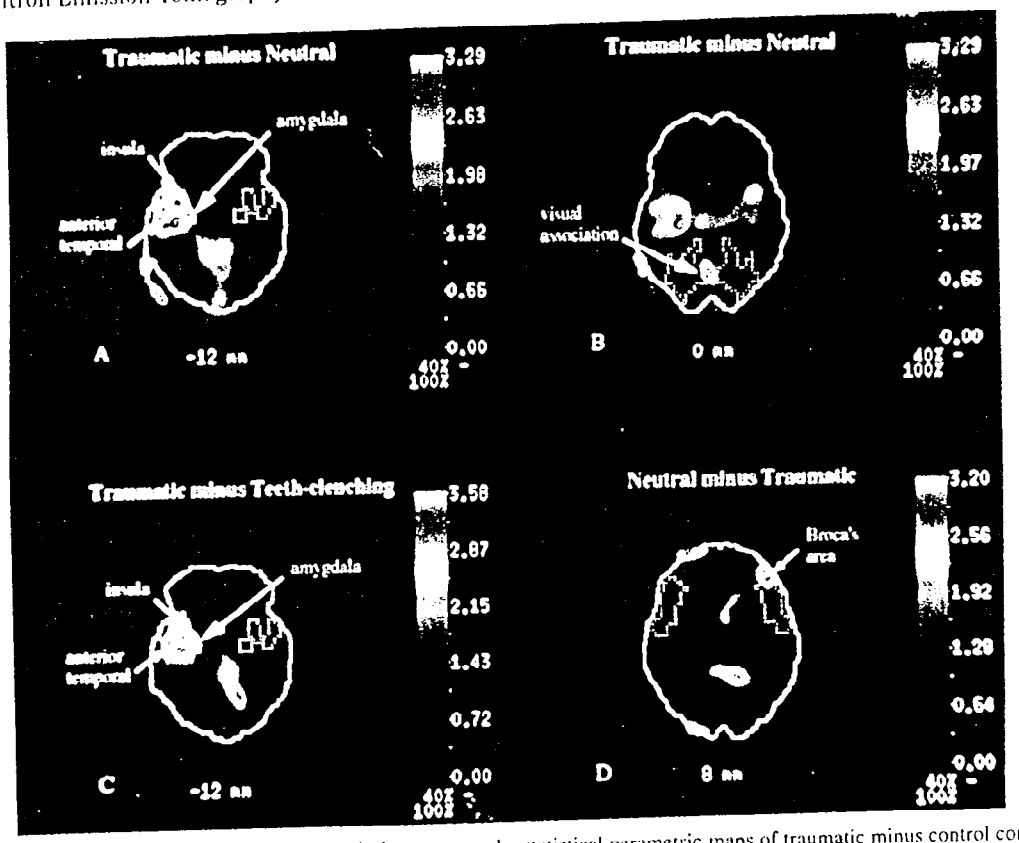
Liberzon and colleagues took single photon emission computed tomography (SPECT) images of Vietnam veterans with and without PTSD after exposing them to either nonspecific 60-cycle noise or to combat sounds. In the Vietnam veterans *without* PTSD, there was increased activation of the anterior cingulate in response to the combat sounds, but not to the running water, while in the subjects with PTSD there was no differential activation of this area.

Pre- versus posttreatment activation. We recently completed a pilot study utilizing eye movement desensitization and reprocessing (ERDR) in which the PTSD scores, as measured by the Clinician Administered PTSD Scale, dropped from an average of 84 to 36. After effective treatment, the subjects registered increased activity in the anterior cingulate bilaterally as well as in the left prefrontal cortex as measured by SPECT images (van der Kolk BA, et al. 1997. Unpublished data).

Implications of Neuroimaging Findings

These neuroimaging studies of patients with PTSD have revealed a number of unexpected findings that may

Figure 1. Positron Emission Tomography of Patients With Posttraumatic Stress Disorder*



*Reprinted with permission from Rauch.[58] Positron emission tomography statistical parametric maps of traumatic minus control conditions for 8 subjects (16 scans per condition) are displayed with a Sokoloff color scale in units of z score. White dashed outlines reflecting the boundaries of specified brain regions, as defined via a digitized version of the Talairach atlas, are superimposed for anatomical reference. Whole-brain slice outlines are demarcated with solid lines. All images are transverse sections parallel to the intercommissural plane, shown in conventional neuroimaging orientation (top = anterior, bottom = posterior, right = left, left = right). Each transverse section is labeled with its z coordinate, denoting its position with respect to the intercommissural plane (superior > 0). For the traumatic minus neutral condition, activation is located within right anterior temporal and insular cortex, the amygdala (panel A), and secondary visual cortex (panel B). Panel C, for the traumatic minus teeth-clenching condition, the pattern of activation shown parallels that seen in panel B. Panel D, for the neutral minus traumatic condition, activation is located within left Broca's area (representing a decrease in relative blood flow associated with traumatic condition).

affect how we conceptualize PTSD. As more results become available, neuroimaging studies may force us to re-evaluate appropriate therapeutic interventions as well.

Activation of the amygdala and related structures. Of the various results, increased activation of the amygdala in response to traumatic scripts is the least surprising. The amygdala has been shown to play a role in the evaluation of the emotional meaning of sensory input: confrontation with feared stimuli activates the amygdala and related structures.[63,64] The amygdala guides emotional behavior by projections to the hypothalamus, hippocampus, and basal forebrain.[64-66] Activation of the amygdala probably mediates the autonomic activation that results from exposure to traumatic scripts[8]: information evaluated by the amygdala is passed on to areas in the brain stem that control behavioral autonomic and neurohormonal response systems.[63] By way of these connections, the amygdala transforms sensory stimuli into physiologic signals that initiate and control emotional responses.

Decrease in hippocampal volume. It is likely that the decreased size of the hippocampus in PTSD is a long-term effect of intrusive reliving of the trauma in body and mind, which is most likely mediated by cortisol-induced hippocampal cell damage.[37] In animals, decreased hippocampal functioning causes behavioral disinhibition by promoting the definition of incoming stimuli in the direction of fight/flight responses.[65] Hence, this may play a role in the ongoing dissociation and misinterpretation of information in the direction of threat, as has been noted in patients with PTSD. In addition, high-level stimulation of the amygdala can also interfere with hippocampal functioning.[67] Hippocampal damage combined with high levels of emotional arousal may prevent the proper evaluation and categorization of experience. This might account for the observation that patients with PTSD have difficulties "taking in" and processing arousing information and learning from such experiences. Their altered biology may make them vulnerable to react to newly arousing

Table 2. Properties of Left Hemisphere

Organizes problem-solving tasks into well-ordered set of operations and processes information in sequential fashion
Involved in perceiving and generation of symbolic representation by breaking down a stimulus into categorical elements and combining them into novel images
Manipulates words and symbols that transcribe personal experience into culturally shared meaning
Generativity is the distinguishing feature of left hemisphere cognition

Table 3. Properties of Right Hemisphere

Involved in the expression and comprehension of global nonverbal emotional communication (tone of voice, facial expression, visual/spatial communication)
Early maturation of right hemisphere consistent with importance of emotional communication early in life
Diffuse representational format, allowing a dynamic and holistic integration across sensory modalities
May by particularly integrated with the amygdala: emotional significance—fear and hostility
Has, at best, a rudimentary capacity to think or communicate analytically, employ syntax, or reason

stimuli as a threat, and to react with aggression, or withdrawal, depending on their premorbid personality.

Hemispheric lateralization. The finding of right hemispheric lateralization in subjects exposed to their personalized trauma scripts suggests that there is differential hemispheric involvement in the processing of traumatic memories. Coupled with Teicher's findings of impaired left hemisphere functioning in traumatized children,[51–56] these findings may have important ramifications for understanding the nature of PTSD. Tables 2 and 3 summarize the relative functions of the two hemispheres. The right hemisphere is involved in the expression and comprehension of global nonverbal emotional communication (tone of voice, facial expression, visual/spatial communication). The early maturation of the right hemisphere is consistent with the importance of emotional communication early in life. The right hemisphere has a diffuse representational format, which allows for a dynamic and holistic integration across sensory modalities.[68,69]

It has been suggested that the right hemisphere is well integrated with the amygdala. This might mediate its association with designating emotional significance to incoming stimuli and regulating the autonomic and hormonal responses to emotional information. While this hemisphere may be sensitive to emotional nuances, it has, at best, a rudimentary capacity to think or communicate analytically, to employ syntax, or to reason.[69–71]

In contrast to the right, the left hemisphere is thought to organize problem-solving tasks into a well-ordered set of operations and to process information in a sequential fashion. By breaking down a stimulus into categorical elements and combining them into novel images, it generates symbolic representations. The labeling of perceptions is a left hemisphere function.[71] It is in the area of categorization and labeling of internal states that people with PTSD seem to have particular problems.[16,72]

Research has shown that derealization and depersonalization at the moment of the trauma is an important predictor for the long-term development of PTSD.[73,74] It is possible that failure of left hemisphere functioning during states of extreme arousal plays a role in these dissociative phenomena. Our brain scans demonstrated that during exposure to a traumatic script, there was decreased activation of Broca's area. Since an intact Broca's area is necessary for the labeling of emotions, impairment of this area would make it difficult for traumatized individuals to "understand" what is going on: they experience intense emotions without being able to label their feelings. Their bodies are aroused and fragments of memories may be activated, but the individuals may not be able to communicate what they are experiencing.

If the part of the CNS necessary for generating sequences and for the cognitive categorization of experience is not functioning properly, trauma would be experienced as timeless and ego-alien. The person may feel, see, or hear the sensory elements of the traumatic experience, but he or she may be prevented from being able to translate this experience into communicable language: they may be literally "out of touch with their feelings." Physiologically, they may respond as if they are being traumatized again, but this may be dissociated from semantic knowledge. If the victim experiences depersonalization and derealization he cannot "own" what is happening, and thus cannot take steps to do anything about it.

CONCLUSIONS AND TREATMENT IMPLICATIONS

If emotional arousal is intense and persists over time, the organism may develop conditioned emotional and biological responses that have long-term effects on how it deals with subsequent information. High levels of emotional arousal are likely responsible for the observation that traumatic experiences initially are imprinted as sensations or states of physiologic arousal that often cannot be transcribed into personal narratives.[75] Treatment consists of helping people integrate their trauma into the totality of their lives. It is generally assumed that helping patients involves processing the traumatic information on a symbolic level, through the use of words and symbols, proper categorization, and integration, in hope that this will abolish conditioned physiologic and neurohormonal responses (see the article by Foa, this issue). However, only further research will show to what degree putting the experience into words is a prerequisite for helping people overcome their trauma. Only careful investigations can elucidate to what degree the biological changes caused by trauma can be reversed by psychological processing of the event.

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